

Application Serial No.: 10/522,826  
Attorney Ref: 63619.US / 6710.4  
Client Ref: LGFILGRASTIM  
(LB/G-32991A/LEK)

R E M A R K S

Claims 1, 3-7, 10, 12-17, 19-21, and 23-26 are in the application. Claims 8-9, 11, 18, 22, 28, and 32-37 are canceled. Claims 2, 27, and 29-31 are withdrawn from consideration as being drawn toward a nonelected invention.

In the office action, claims 1, 3-10, 12-17, and 19-26 were rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claim 1 was rejected under 35 U.S.C. §102(b) as allegedly anticipated by Weickert et al. (*Applied and Environmental Microbiology*, 63(11): 4313-4320, November 1997). Claims 1, 3-10, 12-17, and 19-26 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by or, in the alternative, under 35 U.S.C. 103(a), as allegedly obvious over Jeong et al. (*Protein Expression and Purification* 23:311-318, November 2001).

Claims 1, 3-7, 10, 12-17, 19-21, and 23-26 are amended herein to more particularly point out and distinctly define the presently claimed subject matter, and to provide grammatical improvements. Support for the amendments may be found throughout the specification and claims as originally filed. No new matter is added into the case by the present amendments.

All objections and rejections are respectfully traversed. Reconsideration and favorable action are requested in light of the forgoing amendments and these remarks.

A. Claims 1, 3-7, 10, 12-17, 19-21, and 23-26 are Definite.

With respect to the rejection of Claims 1, 3-10, 12-17, and 19-26 under 35 U.S.C. §112, second paragraph. Applicants would like to point out the cancellation of claims 8, 9, and 22. Accordingly, the present remarks will only address the rejection of claims 1, 3-7, 10, 12-17, 19-21, and 23-26 as allegedly indefinite.

According to MPEP 2111.01, the words of a claim must be given their plain and ordinary meaning according to the understanding of those of ordinary skill in the art, unless such meaning is inconsistent with the specification. The specification sets forth on pages 7-8 and 10-11 specific definitions of terms used throughout this application and in the claims. In accordance with the MPEP, the terms defined on pages 7-8 and 10-11 are to be understood as defined in the specification.

According to MPEP 2173.02, definiteness of claim language must be analyzed, not in a vacuum, but in light of:

- (A) The content of the particular application disclosure;
- (B) The teachings of the prior art; and
- (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claims as a whole and the specification to determine whether the claim in question reasonably apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing a sufficiently clear warning to others as to what constitutes infringement of the patent. See, e.g., Solomon v. Kimberly-Clark Corp., 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). See, also In re Larsen, No. 01-1092 (Fed. Cir. May 9, 2001) (unpublished) (The preamble of the Larsen claim recited only a hanger and a loop but the body of the claim positively recited a linear member. The court observed that the totality of all the limitations of the claim and their interaction with each other must be considered to ascertain the inventor's contribution to the art. Upon review of the claim in its entirety, the court concluded that the claim at issue apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, paragraph 2.). See, also, Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings, 370 F.3d 1354, 1366, 71 USPQ2d 1081, 1089 (Fed. Cir. 2004) ("The requirement to 'distinctly' claim means that the claim must have a meaning discernible to one of ordinary skill in the art when construed according to correct principles....Only when a claim remains insolubly ambiguous without a discernible meaning after all reasonable attempts at construction must a court declare it indefinite.").

Applicants respectfully submit that the Examiner has failed to discharge the Examiner's burden of showing the terms of the claims lack sufficient clarity under the law. See MPEP 2173.02, which states that the Examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph, is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. When the Examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the Examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define the patentable subject matter with a

reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the Examiner might desire. Accordingly, it is the burden of the Examiner to at least make a *prima facie* showing that the claim terms rejected/objection to lack sufficient clarity under the law.

Claim 1 is rejected as indefinite for allegedly omitting essential steps. While it is believed that the claim as written was section 112-compliant, claim 1 is amended herein to more clearly recite the active steps of the claimed process. Support for the amendment can be found in the specification and in the claims as originally filed. For example, claim 1 is amended to include the limitations of original claim 9, which is hereby canceled. Claim 1 is also amended to include steps of performing the process, as described in the paragraph bridging pages 5 and 6 of the specification, on page 16, and in examples 1-12 on pages 16-34. No new matter is added into the case by the amendments. Accordingly, claim 1 as amended is more than sufficiently definite under 35 U.S.C. §112.

Claims 19 and 20 were rejected as indefinite for reciting the allegedly undefined terms "GYST", "GYSP", "LYSP", "LYST", "LBON", and "GYSPON" as limitations. According to MPEP 2173.01 and 2111.01, Applicants may (within reason) define in the claims what they regard as their invention essentially in whatever terms they choose so long as any special meaning assigned to a term is clearly set forth in the specification. In this regard, Applicants would like to point out that all of the above terms are explicitly defined on page 14 of the specification. Also, claim 19 is amended to clarify that the composition of the cultivation medium may be selected from among the recited compositions. The amendment is supported by page 14 of the specification. Accordingly, amended claims 19 and 20 are not indefinite.

Claim 12 was rejected as allegedly indefinite for what is said to be a lack of antecedent basis for the recited terminology "the inducer". Claim 12 is amended to rectify any deficiency in this regard. No new matter is added by the amendment. Accordingly, amended claim 12 is not indefinite.

Claim 21 was also rejected as allegedly indefinite for lack of antecedent basis for terminology "the additive" recited. Claim 21 is amended to provide proper antecedent basis. No new matter is added by the amendment. Accordingly, amended claim 21 is not indefinite.

Claims 3-7, 10, 13-17, and 23-26 were rejected as allegedly indefinite for depending from allegedly indefinite base claims. However, it has been shown herein that the base claims are not indefinite, and thus their dependents should also be deemed compliant with §112. Accordingly, reconsideration and allowance of claims 1, 3-7, 10, 12-17, 19-21, and 23-26 are hereby respectfully requested.

**B. Claim 1 is Patentable Over the Cited Reference.**

Claim 1 was rejected as allegedly anticipated by Weickert et al. (Applied and Environmental Microbiology, 63(11):4313-4323, November 1997). Claim 1 is an independent claim directed to a process for the production of a biologically active protein. The protein is expressed as a heterologous protein in inclusion bodies in an expression system comprising a cultivated organism. One or more cultivation parameters are regulated to affect (e.g. increase) the aqueous solubility (and thus the proportion of correctly folded, biologically active protein) of the inclusion bodies. The inclusion bodies are then isolated, optionally washed, and solubilized under non-denaturing conditions. The biologically active protein is then purified from the solubilized inclusion bodies.

Weickert teaches that the stabilization of apoglobin by lowered temperature during fermentation leads to an increased yield of soluble recombinant hemoglobin in *E. coli*. However, Weickert does not teach that soluble protein is expressed as a protein precursor in inclusion bodies, as called for in claim 1. Weickert is merely concerned with hemoglobin that is already soluble and not present in the inclusion bodies, which he teaches are insoluble and comprised of insoluble protein aggregates. Thus, no teaching or disclosure is provided in Weickert for treating soluble inclusion bodies under non-denaturing conditions prior to purification of the protein, as called for in claim 1. It is well established that in order for a reference to anticipate a claim, the reference must contain each and every element and limitation found in the claim. Since Weickert does not disclose at least the aforementioned limitations of claim 1, the claim is plainly not anticipated by Weickert. Reconsideration and allowance of claim 1 are hereby respectfully requested.

**C. Claims 1, 3-7, 10, 12-17, 19-21, and 23-26 are Patentably Distinct from the Cited Reference**

Claims 1, 3-7, 10, 12-17, 19-21, and 23-26 were rejected as allegedly being anticipated by, or in the alternative, obvious over Jeong et al. (Protein Expression and Purification 23:311-318, November 2001). It is submitted that this rejection is also not well taken because, among other things, a reference cannot properly be said to either anticipate a claim or render a claim obvious unless it is shown to contain all of the elements or limitations in the claim. Plus, it must be shown that a person of ordinary skill in the art would have found it "obvious" to put those elements and limitations together in the manner called for in the claim.

Claim 1 is an independent claim, from which all the remaining claims depend. Claim 1 calls for, among other things, expressing a biologically active protein in an expression system comprising a cultivated organism. The protein is expressed as a protein precursor in inclusion bodies, which are then isolated, optionally washed, and solubilized under non-denaturing conditions before purifying the biologically active protein.

Jeong teaches the secretory production of hG-CSF in *E. coli*, which is an entirely different process from that called for in claim 1. In Jeong, the hG-CSF is fused with a signal sequence in order to direct the protein to be secreted in the periplasm. In order to recover the hG-CSF, the fusion protein is said to be digested with a restriction enzyme to cleave the signal sequence and provide a biologically active hG-CSF. The peptides of Jeong are not accumulated as biologically active proteins in inclusion bodies, as called for in claim 1. Nor does Jeong teach the regulation of one or more cultivation parameters in order to affect the aqueous solubility of the inclusion bodies. For at least these reasons, Jeong does not anticipate or render obvious claim 1.

Claims 3-7, 10, 12-17, 19-21, and 23-26 depend from claim 1 and add further elements and limitations thereto, also not disclosed in or obvious from the cited reference. According to the MPEP, if a base claim is allowable, then all of its dependents are also allowable. Since the aforementioned claims all depend from claim 1, which has been shown to be patentable over the reference, then the dependent claims should also be allowable. Reconsideration and allowance of claims 1, 3-7, 10, 12-17, 19-21, and 23-26 are hereby respectfully requested.

## CONCLUSION

Finally, it is advised in the office action that if claim 3 is found to be allowable, then claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. Since

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claim 3 is believed to be allowable, upon receipt of a Notice of Allowance, Applicants represent that they will file a further amendment requesting cancellation of claim 4.

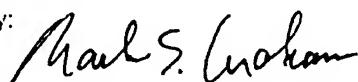
Also, upon the allowance of claim 1, rejoinder of the non-elected species of claim 3 will be requested.

Applicants respectfully submit that a full and complete response to the office action is provided herein, and that the application is now fully in condition for allowance. Action in accordance therewith is respectfully requested.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our Deposit Account No. 122355.

Respectfully submitted,  
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